REMARKS

I. Preliminary Comments

The present invention relates generally to immunotherapy methods providing reduced risk of anaphylaxis. In particular, the invention is directed to the preparation of improved compositions of contiguous overlapping peptide fragments (COPs) for selected allergens wherein the fragments are capable of inducing a T cell response in patients who are hypersensitive to the allergen but wherein administration of the compositions of the invention results in lower levels of IgE stimulation activity.

According to this method, COPs are generated by the steps of: (1) determining candidate contiguous overlapping peptides by a method comprising: (a) conducting a structural analysis of the selected allergen; (b) selecting one or more separation sites to provide contiguous overlapping peptide fragments greater than 30 peptides in length which are linear and which peptides overlap each separation site; (2) producing said candidate contiguous overlapping peptide fragments; and (3) screening said candidate COPs by the steps of: (a) selecting COPs characterized by having a T cell stimulating activity for T cells specific for the selected polypeptide allergen which is greater than a selected minimum; and (b) selecting COPs characterized by having an IgE binding activity for IgE's reactive with the selected polypeptide allergen which is less than a selected maximum.

The claims have been amended in order to add clarity and provide antecedent basis for various of the recited elements. No new matter is introduced thereby

II. Outstanding Rejections

Claims 55-65 stand rejected under 35 U.S.C. §112 (first paragraph) as lacking written descriptive support.

Claims 55-65 stand rejected under 35 U.S.C. §112 (first paragraph) as containing subject matter which was not enabled by the disclosure.

Claims 55-61 stand rejected under 35 U.S.C. §102 (b) as being anticipated by Kammerer et al., Clin. Exper. Allergy 27:1016 (1997).

Claims 55 and 63-65 stand rejected under 35 U.S.C. §103(a) over the combination of Kammerer and Spertini et al., Abstract AAAI presented March 3-8 (2000) J. Allergy Clin. Immunol. 105 (1-pt.2) S278 (C23).

Claims 55 and 61-62 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kammerer in view of Shanti et al., Cell Mil. Life Sci. 61:525-536 (2004).

III. Patentability Arguments

The claims as amended above should be allowed in light of the foregoing amendments and for the reasons set out below.

A. The Written Description Rejection of Claims 55-65 Under 35 U.S.C. §112 (first paragraph) Should be Withdrawn.

The rejection of claims 55-65 for lack of written description under 35 U.S.C. 112 (first paragraph) should be withdrawn for the following reasons and in light of the amendments made herein. The specification provides disclosure of each of the recited elements in the claims. Specifically, support for the step of conducting a structural analysis of the selected allergen is provided in para [0052] while the step of selecting one or more separation sites to provide contiguous overlapping peptide fragments greater than 30 peptides in length which are linear (para. [0038]) is taught at para [0020]. The steps of producing and screening candidate COPs for T cell stimulating activity is taught at para. [0057], and the step of selecting COPs characterized by having an IgE binding activity for the selected polypeptide antigen which is less than a selected maximum is taught at paras. [0038], [0056], [0314] and [0315].

Not only does the specification provide written descriptive support for the elements of independent claim 55 but the dependent claims are supported as well. The rejection of claim 56 on the basis that "holoprotein" is not taught should be withdrawn in light of the disclosure of the specification of paras [0036-0037] that would clearly be understood by the ordinarily skilled worker as comparing reduced IgE activity and conserved T cell activity compared to the native allergen which is a holoprotein. Nevertheless, claim 56 has been amended to delete the recitation of "holoprotein" in order to expedite allowance of the claims.

The rejection of dependent claims 57 and 58 on the basis that the specification **does disclose** the elements of 10 to 15 residue overlaps and **does disclose** a T cell stimulating index of greater than 2 but only teaches ***in vivo*** **use** should be withdrawn because the worker of ordinary skill would appreciate that the specification teaches screening to identify useful peptide fragments for therapy.

The rejection of dependent claims 59 and 60 directed to generating COPs which are useful in inducing tolerance and which are useful in desensitization immunotherapy should similarly be withdrawn in light of the teaching of those methods at paras [0020], [0023], [0045] and [0064] and elsewhere throughout the specification.

Further, the recitation in claims 61-65 of measurement of IgE binding activity by immunoblotting, dot blotting or dermal tests is supported at paras. [0181], [0155], [0134] [0022] and [0132] and would have been understood by those of ordinary skill to be part of a process of identifying useful COPs.

The rejection on the basis that written descriptive support is not provided for generating an improved COP composition for a **selected polypeptide allergen** should be withdrawn because the invention described **is a method** the practice of which need not have been completed in order to be described! The issue of written description is one of whether those of ordinary skill would recognize that the applicant was in possession of his or her invention at the time an application was filed. (See MPEP 2163 I.) In the situation of a screening method, it is not necessary for purposes of adequate written description that the

results of such a screening be presented for every possible analyte to be tested. Thus, Applicants do not claim a genus comprising all COPs which are the **results of their method** for generating COP compositions, they claim a method! Such a universal collection of COPs was unknown at the time of Applicants' filing and was not described therein.

Applicants have not provided a universal collection of COPs and their claims are not directed to such a universal collection of COPs. Instead, their invention and claims are directed to a series of steps (a method) to be carried out for identifying such COPs. The proper question before the Office is whether Applicants' revealed by their written disclosure that they were in possession of such a method at the time their application was filed. In this case, it is clear that Applicants were in possession of such a method.

B. The Lack of Enablement Rejection of Claims 55-65 Under 35 U.S.C. §112 (first paragraph) Should be Withdrawn because the Invention is the Method and not the Result.

The rejection of claims 55-65 for lacking enablement under 35 U.S.C. 112 (first paragraph) should be withdrawn because the disclosure is enabling for practice of the claimed method which neither predicts nor guarantees any particular result. As discussed with respect to the issue of written description, Applicants do not claim the **result** of their analysis *e.g.*, a collection of COPs for every known allergen. Instead, they claim (and they enable) a method for identifying improved compositions of COPs. Just as the results of a screening method for a pathogen or a receptor binding site are not known prior to actual practice of the method, the results of the inventive method are also unknown prior to its practice.

Applicants' method includes at least two selection steps by which it screens candidate COPs. That neither step is guaranteed is not a failure of enablement any more than a negative screening result for detection of a pathogen or receptor binding site establishes lack of enablement for those screening methods. Accordingly, there is no failure of enablement of the claimed invention.

That aspect of the rejection which argues that there lacks guidance for conducting a structural analysis of the selected allergen should be withdrawn as those of ordinary skill informed by the disclosure of para. [0052] would be equipped to carry out such an analysis using tools and methods well known to the art. Further, those of ordinary skill would be enabled to select one or more separation sites to provide contiguous overlapping peptide fragments greater than 30 peptides in length which are linear.

The screening step which follows is enabled because it is not necessary to know beforehand what the result of that screening step will be. The fact that the result of a screening step is unknown before it has been conducted is not a proper basis for a lack of enablement rejection. It is thus unnecessary to know the correlation between structure and IgE binding **before** conducting the assay because the assay will provide the result. Even though the results of such assays are unknown beforehand, screening to identify those peptide fragments having reduced IgE binding (and those that do not) is not beyond the ordinary skill in the art.

Applicants do not claim induction of desensitization and/or tolerance to a specific allergen "by any allergen-specific immunotherapy." Instead, they claim and enable a method for identifying improved compositions of COPs. Accordingly, the rejection under 35 U.S.C. §112 (first paragraph) for lack of enablement should be withdrawn.

C. The Indefiniteness Rejections of Claims 55-65 Under 35 U.S.C. §112 (second paragraph) Should be Withdrawn in light of the Amendments to the Claims.

The rejection of claims 55-65 for indefiniteness under 35 U.S.C. 112 (first paragraph) should be withdrawn in light of the amendments submitted herewith.

D. The Rejection of Claims 55-61 Under 35 U.S.C. §102(b) over Kammerer et al., Should be Withdrawn.

The rejection of claims 55-61 under 35 U.S.C. §102(b) over Kammerer et al., Clin. Exper. Allergy 27:1016 (1997) should be withdrawn because Kammerer fails to teach a method of selecting COPs based upon the combination of performing T cell stimulation and IgE binding tests to obtain such COPs. Moreover, Kammerer Figure 1 depicts mapping of

PLA_2 with short and long peptides but fails to teach the step of conducting a "structural analysis" of the allergen. In addition, Kammerer fails to disclose a step of "selecting one or more separation sites as required by the claims.

For these reasons, the anticipation rejection over Kammerer should be withdrawn.

E. The Rejection of Claims 55 and 63-65 Under 35 U.S.C. §103(a) over Kammerer et al., and Spertini Should be Withdrawn.

The rejection of claims 55 and 63-65 under 35 U.S.C. §103(a) over Kammerer et al., and Spertini et al., Abstract AAAI presented March 3-8 (2000) J. Allergy Clin. Immunol. 105 (1-pt.2) S278 (C23) should also be withdrawn because Kammerer fails to disclose or teach the elements of independent claim 55 and Spertini fails to make up for those deficiencies of disclosing conducting a structural analysis or of selecting one or more separation sites.

F. The Rejection of Claims 55 and 61-62 Under 35 U.S.C. §103(a) over Kammerer et al., and Shanti et al., Should be Withdrawn.

The rejection of claims 55 and 61-62 under 35 U.S.C. §103(a) over Kammerer et al., and Shanti et al., Cell Mil. Life Sci. 61:525-536 (2004) should be withdrawn because Shanti fails to make up for the deficiencies of Kammerer with respect to independent claim 55 as described above.

Moreover, Shanti teaches away from the present invention by teaching that one of ordinary skill would have performed dot blots for showing the presence of IgE able to bind to COPs Unexpectedly, COPs do not bind under comparable experimental conditions to serum IgEs of allergic patients. Thus, the method of the claimed invention provides the selection of peptides which, contrary to Shanti's peptides, do not bind IgE on dot blots! Accordingly, the rejection of claims 55 and 61-62 should be withdrawn.

CONCLUSION

In view of the above amendments and for the reasons set out, Applicants believe that each of claims 55-65 are in condition for allowance. Should the Examiner wish to discuss any issue of form or substance she is encouraged to contact the undersigned attorney at the number listed below.

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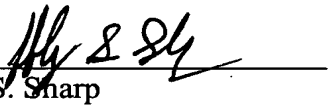
Respectfully submitted,

By 

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